REMARKS

Claims 1 and 2 are pending in this application. Claims 1 and 2 have been rejected. Claim 2 has been amended. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Rejection of Claims Under 35 U.S.C. 103(a)

Claims 1 and 2 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Dalton et al. (US 2003/0004140), Rapaport (U.S. Patent No. 5,049,372), and Altaba et al. (US 2005/0130922). The Examiner suggests that Dalton et al. teach a method of treating cancer comprising administering an effective amount of bisphosphonate, thereby enhancing the efficacy of a chemotherapeutic and/or radiation treatment, where the chemotherapeutic is the targeting agent. The Examiner suggests further that Rapaport teaches a method of treating cancer comprising administering an effective amount of adenosine monophosphate, while Altaba teaches use of deoxycoformycin to treat cancer. The Examiner suggests, therefore, it would have been *prima facie* obvious for one of skill in the art to modify the method of

Dalton to include the adenosine monophosphate of Rapaport and the deoxycoformycin of Altaba, with motivation provided by the fact that all the methods cited are methods for treatment of cancer which is a disease associated with bone metastasis. Applicant respectfully disagrees with the Examiner's suggestions concerning this combination of prior art.

To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP 2143. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all claim limitations.

Dalton et al. (US 2003/0004140) is a patent application that discloses methods for treating cancer including use of bisphosphonate to disrupt cancer cell adhesion. The patent application discusses use of bisphosphonate with doxorubicin, a chemotherapeutic agent, as well as with radiation treatment. Nowhere does this patent, either alone or when combined with the other cited references, demonstrate the successful use in patients of bisphosphonate in a combination therapy with any targeting agent

or any adenosine agent or an adenosine receptor blocking agent for treatment of metastasis of cancer of any type. Although Rapaport (U.S. Patent 5,049,372) teaches use of ATP or adenosine agents to treat cancer, nowhere does this patent teach or suggest successful combination therapy for treatment of cancer in a patient where the combination therapy is ATP and bisphosphonate and a targeting agent as defined in the specification as filed. Most importantly, although the Examiner suggests that Altaba discloses a method for treating cancer comprising administering an agent that blocks adenosine receptors, this patent application does not disclose such a method; this patent application discloses use of an adenosine deaminase inhibitor, not a receptor blocker.

Therefore, either alone or when combined, the cited references fail to teach successful combination therapy with an adenosine agent, bisphosphonate, and a targeting agent, with or without an adenosine receptor blocker. It is only with the specification in hand that one of skill would see that these different agents could be successfully combined to treat cancer, specifically bone metastasis. Therefore, one of skill would have no expectation of success in treating bone metastasis as claimed because the cited references do not demonstrate such clinical use. MPEP is quite

clear that the fact that references can be combined or modified is not sufficient to establish *prima facie* obviousness (In re Mills, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990)). Nowhere does the cited references suggest the combination as claimed and thus cannot have shown successful use clinically of the combination. In clinical medicine, it is well established that one cannot predict the efficacy of a combination merely based on results of each individual compound. Instead, it must be shown that the agents, when combined, have efficacy, without unwanted toxicity. It is only with the specification in hand that one of skill is provided with such data and assurances. Accordingly, the combination of prior art cannot make obvious the instant invention and withdrawal of this rejection is respectfully requested.

II. Conclusion

Applicant believes that the foregoing comprises a full and complete response to the Office Action of record. Accordingly,

favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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